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- **Table 1: Details of physiological and behavioural changes reported in scientific studies on rabbit pain and analgesia** (NZW=New Zealand White, IV= Intravenous, IM=Intramuscular, SC=Subcutaneous, PO=Orally, d=Day, q12h=Every 12 hours, q24h=Every 24 hours, SRB= Compounded sustained-release formulation of buprenorphine, FCM= Faecal corticosterone metabolites)

| Study              | Rabbit number/Breed | Procedure                                     | Analgesia   | Physiological parameters  | Outcome  | Behavioural parameters   | Outcome  | Comments  |
|--------------------|---------------------|---|---|---|--|--|--|---|
| Cooper et al. 2009 | 29/Dutch Belted     | Ovariohysterectomy                            | 3 groups: <ul style="list-style-type: none"> <li>• Buprenorphine 0.03 mg/kg IM q 12h for 2 d</li> <li>• Meloxicam 0.2 mg/kg SC q 24h for 2 d</li> <li>• 0.5% bupivacaine infused locally at the incision</li> </ul>         | <ul style="list-style-type: none"> <li>• Haematology</li> <li>• Biochemistry</li> <li>• Body temperature</li> <li>• Body weight</li> <li>• Faecal output</li> <li>• Faecal flora</li> </ul> | <ul style="list-style-type: none"> <li>• No changes in body temperature, haematology, biochemistry and faecal flora during the study</li> <li>• Decrease in body weight and faecal output</li> </ul> | <ul style="list-style-type: none"> <li>• Food intake</li> </ul>  | <ul style="list-style-type: none"> <li>• Decrease in food intake</li> </ul>  | The changes in body weight, faecal output and food intake were found to be more severe when bupivacaine was used. |
| Leach et al. 2009  | 28/NZW              | Ovariohysterectomy                            | 4 groups: <ul style="list-style-type: none"> <li>• Meloxicam 0.2 mg/kg PO (Loading dose)</li> <li>• Meloxicam 0.6 mg/kg PO (Loading dose)</li> <li>• Meloxicam 1mg/kg PO (Loading dose)</li> <li>• Control group</li> </ul> | <ul style="list-style-type: none"> <li>• Body weight</li> </ul>   | <ul style="list-style-type: none"> <li>• Decrease in body weight in all animals</li> </ul>   | <ul style="list-style-type: none"> <li>• Inactive pain behaviour (Twitch, wince, stagger, flinch, press, pain, adjust low, shuffle)</li> <li>• Other behaviours (e.g. grooming, ear position, cage position, head shaking, etc)</li> </ul> | <ul style="list-style-type: none"> <li>• Increased inactive pain behaviour</li> <li>• Minimal differences of the Other behaviours</li> </ul> | Inactive pain behaviour was considered the most indicative of all the behaviours assessed during the study        |
| Weaver et al. 2010 | 20/NZW              | Ovariohysterectomy and telemeter implantation | 4 groups: <ul style="list-style-type: none"> <li>• Buprenorphine 0.02 mg/kg</li> </ul>  | <ul style="list-style-type: none"> <li>• Body weight</li> <li>• Faecal output</li> </ul>  | <ul style="list-style-type: none"> <li>• Body weight decreased significantly in all animals</li> </ul>   | <ul style="list-style-type: none"> <li>• Food and water intake</li> </ul>  | <ul style="list-style-type: none"> <li>• Food and water intake decreased significantly in</li> </ul>   | No statistical difference amongst the three   |

|                       |       |   |   |   |  |   |   |   |
|-----------------------|-------|---|---|---|--|---|---|---|
|                       |       |   | <ul style="list-style-type: none"> <li>SC q12h for 3 d</li> <li>Fentanyl 25-µg patch placed 24h prior surgery</li> <li>Ketoprofen 1mg/kg SC q 24h for 3 d</li> <li>Control group</li> </ul>                               |   | <ul style="list-style-type: none"> <li>postoperative up to 7 days.</li> <li>Faecal output decreased significantly in all animals postoperatively</li> </ul>  | <ul style="list-style-type: none"> <li>Travel distance</li> <li>Rearing activity</li> </ul>   | <ul style="list-style-type: none"> <li>all animals postoperatively</li> <li>Travel distance and rearing activity decreased significantly in all animals postoperatively</li> </ul>  | analgesic groups and the control group were found during the study  |
| Farnworth et al. 2011 | 7/NZW | Abdominal implantation of a telemetric device | <p>All animals:</p> <ul style="list-style-type: none"> <li>Carprofen 2 mg/kg SC once</li> </ul>   | -   | -  | <ul style="list-style-type: none"> <li>Several behaviours were recorded post operatively (e.g. grooming, exploring, lying, etc)</li> </ul>                    | <p>Decreased behaviours:</p> <ul style="list-style-type: none"> <li>Grooming</li> <li>Food and water intake</li> <li>Exploring</li> <li>Stretching</li> <li>Others</li> </ul> <p>New behaviours:</p> <ul style="list-style-type: none"> <li>Full-body flex</li> <li>Hind leg shuffle</li> <li>Tight huddle</li> </ul> <p>Increased behaviours:</p> <ul style="list-style-type: none"> <li>Lying</li> <li>Drawing back</li> <li>Staggering</li> <li>Closed eyes</li> </ul> | The authors stated that behavioural indicators of pain may differ depending on housing and surgical procedure |
| Keating et al. 2012   | 8/NZW | Ear tattooing                                 | <p>4 groups:</p> <ul style="list-style-type: none"> <li>Sham tattooing with EMLA cream®</li> <li>Sham tattooing without EMLA cream®</li> <li>Tattooing with EMLA cream®</li> <li>Tattooing without EMLA cream®</li> </ul> | <ul style="list-style-type: none"> <li>Heart rate</li> <li>Arterial blood pressure</li> <li>Serum corticosterone concentration</li> </ul> | <p>All the animals tattooed without EMLA cream:</p> <ul style="list-style-type: none"> <li>Increased heart rate</li> <li>Increased arterial blood pressure</li> </ul> <p>All animals with or without the EMLA cream®:</p> <ul style="list-style-type: none"> <li>Increased Serum corticosterone concentration</li> </ul> | <ul style="list-style-type: none"> <li>Facial expression</li> <li>Grooming</li> <li>Movement</li> <li>Rearing</li> <li>Vocalisation and struggling</li> </ul> | <ul style="list-style-type: none"> <li>Increased grooming was noticed only in the animals tattooed without EMLA cream®</li> <li>Movement and rearing decreased in all animals</li> <li>Rearing, vocalisation and struggling was noticed in</li> </ul>   | The Rabbit Grimace Scale developed during this study provides a validated pain assessment tool in rabbits.    |

|                             |        |                              |                  |   |  |   |   |  | animals tattooed without EMLA cream ®   |  |
|-----------------------------|--------|------------------------------|------------------|---|--|---|---|--|---|--|
| Goldschlag<br>r et al. 2013 | 39/NZW | Vascular of the artery       | cut-down femoral | 4 groups: <ul style="list-style-type: none"><li>Buprenorphine 0.03 mg/kg SC q12h for 3 d</li><li>Meloxicam 0.2 mg/kg SC q24h for 3 d</li><li>Buprenorphine 0.01 mg/kg and meloxicam 0.1 mg/kg SC q 24h for 3 d</li><li>Single dose of 0.5 ml of 0.5% bupivacane infused locally</li></ul> | <ul style="list-style-type: none"><li>Faecal corticosterone metabolites (FCM)</li><li>Faecal ouput</li><li>Urine output</li><li>Body weight</li><li>Haematology</li><li>Biochemestr y</li><li>Faecal flora</li></ul> | In the buprenorphine-meloxicam group, FCM did not change while it increased in the other 3 groups<br>In all animals: <ul style="list-style-type: none"><li>Dedreased faecal output</li><li>Normal urine output</li><li>Decreased body weight</li><li>Normal range of haematology and biochemistry</li><li>Normal faecal flora</li></ul> | <ul style="list-style-type: none"><li>Food intake</li></ul>                               | All animals showed a decrease in food intake   | The study suggests that a multimodal approach using a combination of buprenorphine and meloxicam may control pain better than meloxicam or buprenorphine given alone. |  |
| Hedenqvist<br>et al. 2016   | 18/NZW | Bilateral sinus augmentation | axillary         | 2 groups: <ul style="list-style-type: none"><li>Buprenorphine 0.03mg/kg IV and 0.02 mg/kg SC (Loding dose) and carprofen 5 mg/kg SC q 24 h for 4 d</li><li>Buprenorphine 0.03mg/kg IV and 0.02 mg/kg SC (Loding dose) and saline (NaCl)</li></ul>   | <ul style="list-style-type: none"><li>Body weight</li></ul>  | <ul style="list-style-type: none"><li>No difference between the two groups</li></ul>  | <ul style="list-style-type: none"><li>Facial expressions</li></ul>                        | <ul style="list-style-type: none"><li>No differences between the two groups were found</li></ul>                               | Facial expressions such as orbital tightening and ear positions were considered easy to evaluate by inexperienced people during the study                             |  |
| DiVincenti et<br>al. 2016   | 24/NZW | Tibial implants              | titanium         | 2 groups: <ul style="list-style-type: none"><li>Buprenorphine 0.02 mg/kg SC q12 h for 3 d</li></ul>   | -  | -   | <ul style="list-style-type: none"><li>Grimace scale score</li><li>Acivity score</li></ul> | In both groups: <ul style="list-style-type: none"><li>Increased in Grimace score</li><li>Decreased in activity score</li></ul> | The two treatment groups were comparable during the   |  |

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- Compounded  
sustained-  
release  
formulation of  
buprenorphin  
e (SRB) 0.12  
mg/kg once
- 

study with no  
major  
adverse  
affects  
reported